No Additional THMs Should be Considered for Prioritization

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Evidence that THMs as a Group are Not Clearly Shown to Cause Reproductive & Developmental Toxicity

- USEPA & WHO
- Epidemiologic findings
- Toxicological findings

Studies Identified by OEHHA As "Increased Risk" from THM

- Hwang et al., 2008
  - Not significant for 3 endpoints: LCI $\leq$ 1
  - Significant <all birth defects>
    - Low dose only; no dose-response
    - Overall: 5 studies not SS
- Toledano et al., 2005
  - Not significant: LCI < 1
  - Significant <LBW & VLBW>
    - Confounding w/ socio-economic status unadjusted
    - One H_2O district of 3
    - Not significant for 3 districts combined
    - Overall LBW = 2+ v 5-
    - Overall VLBW = 1+ v 3-
- Wright et al., 2004
  - Significant for SGA
    - No dose-response
    - Overall: 3+ v 11-

Studies Identified by OEHHA As "Increased Risk" from THM (cont)

- Windham et al., 2003
  - Not significant <menstrual cycle>: LCI <1
  - Poor participation
  - Self-reporting error
- King et al., 2000
  - Significant <stillbirth, 100 v 50 ppb>
    - No dose-response
    - Overall: 2+ v 2-
- Waller et al., 1998
  - Significant <SAB>
    - 1 of 3 H_2O supplies
    - Savitz et al. (2005) with improved design = Not significant
    - EPA disqualified Waller study
    - Overall: 1+ v 2-

Other Considerations for Prioritization

- Chemical structure of THM group does not suggest reproductive toxicity
- Metabolism of THM group does not suggest reproductive toxicity

National and International Consensus: No Clear Evidence that THMs as a Group Cause Reproductive or Developmental Toxicity

- USEPA, 2006: "…*concludes that a causal link between adverse reproductive health effects and exposure to chlorinated drinking water or DBPs has not been established* …"

- WHO, 2000: "… *existing epidemiological data are insufficient to allow the importance of observed associations of chlorinated water or THMs and adverse reproductive outcomes to be assessed*."

No Clear or Consistent Association Between Reproductive or Developmental Toxicity and THMs as a Group

- Global review (Tardiff et al. 2006*): "…*The updated epidemiological weight of evidence demonstrated that that no associations with DBP exposure exists for over a dozen [reproductive] outcomes*. …"

- Epidemiologic data since 2001:
  - 29 endpoints = no SS association
  - 8 endpoints = no distinction THMs from CBP
  - 3 endpoints = inconsistent findings
  - 1 endpoint = no confirmation, replication, dose-response

- **Reg. Tox Pharm* **45**, 185-205 (2006)

Comprehensive Epidemiologic Factors Do Not Support Prioritization of THM Group

- All negative and positive studies included
- Major study types included
- 40+ endpoints included
- Quality of studies including confounders addressed
- Dose-response sought
- Statistical analyses evaluated
- Criteria for positive associations applied

Toxicology Weight of Evidence = No Clear Cause of Reproductive or Developmental Toxicity by Group of THMs

- No studies

Conclusion

- No sufficient evidence to prioritize any additional THMs either as a group or individually